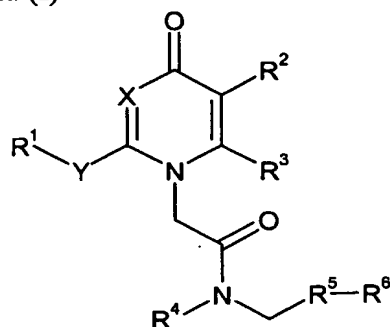


Claims

1. A compound of formula (I)



(I)

in which:

R¹ is an aryl group, optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from C₍₁₋₆₎alkyl, C₍₁₋₆₎alkoxy, C₍₁₋₆₎alkylthio, arylC₍₁₋₆₎alkoxy, hydroxy, halogen, CN, COR⁷, carboxy, COOR⁷, NR⁷COR⁸, CONR⁹R¹⁰, SO₂NR⁹R¹⁰, NR⁷SO₂R⁸, NR⁹R¹⁰, mono to perfluoro-C₍₁₋₄₎alkyl, mono to perfluoro-C₍₁₋₄₎alkoxyaryl, and arylC₍₁₋₄₎alkyl;

R² is halogen, C₍₁₋₃₎alkyl, C₍₁₋₃₎alkoxy, hydroxyC₍₁₋₃₎alkyl, C₍₁₋₃₎alkylthio, C₍₁₋₃₎alkylsulphinyl, aminoC₍₁₋₃₎alkyl, mono- or di-C₍₁₋₃₎alkylaminoC₍₁₋₃₎alkyl, C₍₁₋₃₎alkylcarbonylaminoC₍₁₋₃₎alkyl, C₍₁₋₃₎alkoxyC₍₁₋₃₎alkylcarbonylaminoC₍₁₋₃₎alkyl, C₍₁₋₃₎alkylsulphonylaminoC₍₁₋₃₎alkyl, C₍₁₋₃₎alkylcarboxy, C₍₁₋₃₎alkylcarboxyC₍₁₋₃₎alkyl, and

R³ is hydrogen, halogen, C₍₁₋₃₎alkyl, or hydroxyC₍₁₋₃₎alkyl; or

R² and R³ together with the pyridone or pyrimidone ring carbon atoms to which they are attached form a fused 5- or 6-membered carbocyclic ring; or

R² and R³ together with the pyridone or pyrimidone ring carbon atoms to which they are attached form a fused benzo or heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from halogen, C₍₁₋₄₎alkyl, cyano, C₍₁₋₃₎alkoxyC₍₁₋₃₎alkyl, C₍₁₋₄₎alkoxy or C₍₁₋₄₎alkylthio, or mono to perfluoro-C₍₁₋₄₎alkyl;

R⁴ is (CH₂)_n substituted by a substituent selected from benzimidazole or a 5- or 6-membered heteroaryl, each of which may optionally be substituted by one or more R¹¹;

R⁵ is an aryl or a heteroaryl ring optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from C₍₁₋₆₎alkyl, C₍₁₋

6)alkoxy, C₍₁₋₆₎alkylthio, arylC₍₁₋₆₎alkoxy, hydroxy, halogen, CN, COR⁷, carboxy, COOR⁷, NR⁷COR⁸, CONR⁹R¹⁰, SO₂NR⁹R¹⁰, NR⁷SO₂R⁸, NR⁹R¹⁰, mono to perfluoro-C₍₁₋₄₎alkyl and mono to perfluoro-C₍₁₋₄₎alkoxy;

R⁶ is an aryl or a heteroaryl ring which is further optionally substituted by 1, 2, 3 or 4 substituents which may be the same or different selected from C₍₁₋₆₎alkyl, C₍₁₋₆₎alkoxy, C₍₁₋₆₎alkylthio, C₍₁₋₆₎alkylsulfonyl, arylC₍₁₋₆₎alkoxy, hydroxy, halogen, CN, COR⁷, carboxy, COOR⁷, CONR⁹R¹⁰, NR⁷COR⁸, SO₂NR⁹R¹⁰, NR⁷SO₂R⁸, NR⁹R¹⁰, mono to perfluoro-C₍₁₋₄₎alkyl and mono to perfluoro-C₍₁₋₄₎alkoxy, or C₍₅₋₁₀₎alkyl;

R⁷ and R⁸ are independently hydrogen or C₍₁₋₁₂₎alkyl, for instance C₍₁₋₄₎alkyl (e.g. methyl or ethyl);

R⁹ and R¹⁰ which may be the same or different is each selected from hydrogen, or C₍₁₋₁₂₎alkyl, or R⁹ and R¹⁰ together with the nitrogen to which they are attached form a 5- to 7 membered ring optionally containing one or more further heteroatoms selected from oxygen, nitrogen and sulphur, and optionally substituted by one or two substituents selected from hydroxy, oxo, C₍₁₋₄₎alkyl, C₍₁₋₄₎alkylcarboxy, aryl, e.g. phenyl, or aralkyl, e.g. benzyl, for instance morpholine or piperazine;

R¹¹ is selected from the group consisting of halogen, CF₃, C₍₁₋₆₎alkyl, C₍₁₋₆₎alkoxy C₍₁₋₆₎alkyl or benzyl optionally substituted by CF₃, C₍₁₋₆₎alkyl, C₍₁₋₆₎alkoxy or halogen;

X is CH or nitrogen;

Y is C₍₂₋₄₎alkylene group (optionally substituted by 1, 2 or 3 substituents selected from methyl and ethyl), CH=CH, or (CH₂)_mS;

n is 1, 2, 3 or 4; and

m is 1 or 2,

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein R¹ is phenyl optionally substituted by 1, 2, 3 or 4 halogen substituents.

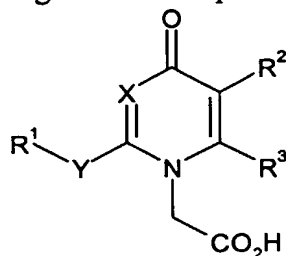
3. A compound according to claim 2 wherein R¹ is phenyl substituted by 1 to 3 fluoro.

4. A compound according to any of claims 1 to 3 wherein X is CH and R² and R³ together with the pyridone ring carbon atoms to which they are attached form an unsubstituted fused benzo or pyrido ring.

5. A compound according to any of claims 1 to 3 wherein X is N and R² and R³ together with the pyrimidone ring carbon atoms to which they are attached form an unsubstituted fused benzo or cyclopentenyl ring.
6. A compound according to any of claims 1 to 5 wherein R⁴ is (CH₂)_n substituted by benzimidazolyl, imidazolyl, thiazolyl, pyrazolyl, tetrazolyl and pyridyl each of which may be optionally further substituted by one or more R¹¹.
7. A compound according to claim 6 wherein the benzimidazolyl, imidazolyl, thiazolyl, pyrazolyl, tetrazolyl or pyridyl ring is unsubstituted or substituted by one or two substituents selected from halogen, C₍₁₋₆₎ alkyl and C₍₁₋₆₎ alkoxyC₍₁₋₆₎ alkyl.
8. A compound according to claim 7 wherein the benzimidazolyl, imidazolyl, thiazolyl, pyrazolyl, tetrazolyl or pyridyl ring is substituted by one or two substituents selected from chloro, fluoro, bromo, C₍₁₋₄₎ alkyl and C₍₁₋₃₎ alkoxy C₍₁₋₃₎ alkyl.
9. A compound according to any claims 1 to 8 wherein R⁵ is phenyl or pyridyl.
10. A compound according to any of claims 1 to 9 wherein R⁶ is phenyl substituted by mono to perfluoro- C₍₁₋₄₎ alkyl, halogen or C₍₁₋₆₎ alkyl.
11. A compound according to any of claims 1 to 10 wherein R⁵ is phenyl and R⁶ is phenyl optionally substituted by trifluoromethyl.
12. A compound according to any of claims 1 to 11 wherein Y is CH₂S or (CH₂)₂.
13. A compound of formula (I) as named in any of Examples 1 to 67.
14. A pharmaceutical composition comprising a compound of formula (I) as defined in any of claims 1 to 13 and a pharmaceutically acceptable carrier, optionally with one or more other therapeutic compounds.
15. A compound of formula (I) as defined in any of claims 1 to 3 for use in therapy.
16. The use of a compound of formula (I) as defined in any of claims 1 to 13 for the manufacture of a medicament for treating atherosclerosis.

17. A method of treating a disease associated with activity of the enzyme Lp-PLA₂ which method involves treating a patient in need thereof with a therapeutically effective amount of a compound of formula (I) as defined in any of claims 1 to 13.

18. A process for preparing a compound of formula (I) as defined in claim 1 which process comprises reacting an acid compound of formula (II):



(II)

in which X, Y, R¹, R² and R³ are as hereinbefore defined, with an amine compound of formula (III):



(III)

in which R⁴, R⁵ and R⁶ are as hereinbefore defined; under amide forming conditions.